Scientific and Technical Information Center

Requester's Full Name: Jeffrey E. Russel Examiner #: 62785 Date: 12-27-2004
Art Unit: 1654 Phone Number 571-272-0969 Serial Number: 10/671,340
Mail Box and Bldg/Room Location: REM 3C18 (mailbox), 3D19 (office) Results Format Preferred (circle): PAPER DISK E-MAIL
If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

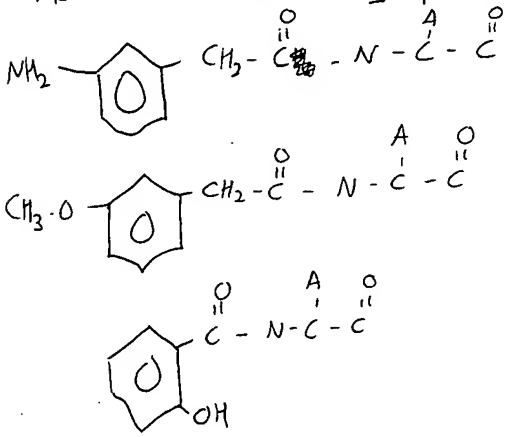
Title of invention: Modified GLP-1 Peptides With Increased Biological Potency

Inventors (please provide full names): D. Gravel, K. Peri, T. Abribat, A. Habi

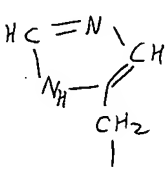
Earliest Priority Filing Date: 9-25-2003

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

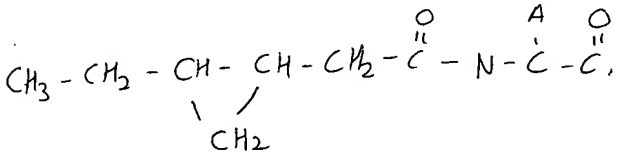
Please search the following partial structures:



If there are many Lit's, please require A to be



(a Histidine side chain



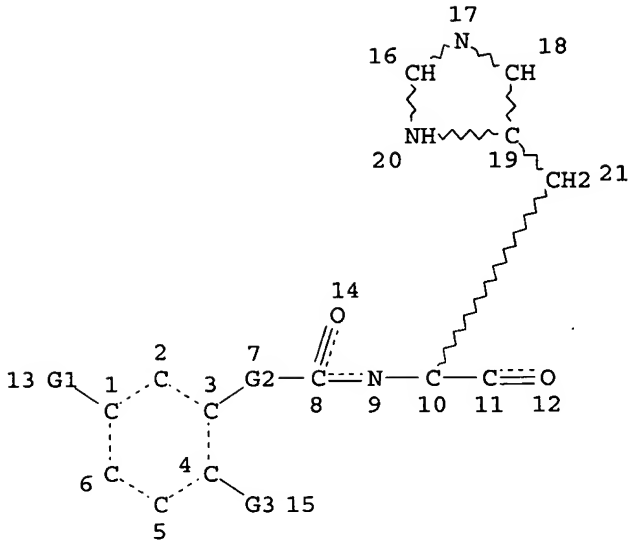
Thank you.

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher:	NA Sequence (#)	STN
Searcher Phone #	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	QuestelOrbit
Date Searcher Picked Up:	Bibliographic	Dr.Link
Date Completed:	Litigation	Lexis/Nexis
Searcher Prep & Review Time	Fulltext	Sequence Systems
Clerical Prep Time:	Patent Family	WWW/Internet
Online Time	Other	Other (specify)

FTO-1590 (8-01)

Russel
10/671340

=> d l5 que stat
L3 STR



VAR G1=H/OME/NH2
REP G2=(0-1) CH2
VAR G3=OH/H
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE
L5 344 SEA FILE=REGISTRY SSS FUL L3

100.0% PROCESSED 84724 ITERATIONS 344 ANSWERS
SEARCH TIME: 00.00.01

=> fil caplus;s l5 and (glp-1 or glucagon like peptide 1 or proglucagon)
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	158.78	158.99

FILE 'CAPLUS' ENTERED AT 13:45:24 ON 30 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Searched by: Mary Hale 571-272-2507 REM 1D86

FILE COVERS 1907 - 30 Dec 2004 VOL 142 ISS 1
FILE LAST UPDATED: 29 Dec 2004 (20041229/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
          312 L5
         2595 GLP
           84 GLPS
         2630 GLP
                (GLP OR GLPS)
      8134322 1
         1696 GLP-1
                (GLP(W)1)
        23447 GLUCAGON
           96 GLUCAGONS
        23459 GLUCAGON
                (GLUCAGON OR GLUCAGONS)
       647478 LIKE
          233 LIKES
       647677 LIKE
                (LIKE OR LIKES)
       321669 PEPTIDE
       235124 PEPTIDES
       411781 PEPTIDE
                (PEPTIDE OR PEPTIDES)
      8134322 1
         1626 GLUCAGON LIKE PEPTIDE 1
                (GLUCAGON(W)LIKE(W)PEPTIDE(W)1)
          415 PROGLUCAGON
           10 PROGLUCAGONS
          416 PROGLUCAGON
                (PROGLUCAGON OR PROGLUCAGONS)
L6            1 L5 AND (GLP-1 OR GLUCAGON LIKE PEPTIDE 1 OR PROGLUCAGON)

=> d cbib abs hitstr

L6   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
2004:287858   Document No. 140:298100  Modified GLP-1
     peptides with increased biol. potency in the treatment of glucose
     metabolism disorders, insulin resistance, and related conditions.  Gravel,
     Denis; Peri, Krishna; Abribat, Thierry; Habi, Abdelkrim (Theratechnologies
     Inc., Can.).  PCT Int. Appl. WO 2004029081 A2 20040408, 47 pp.  DESIGNATED
     STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
     CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH,
     GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
     LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT,
     RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US,
     UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY,
     DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE,
     SN, TD, TG, TR.  (English).  CODEN: PIXXD2.  APPLICATION: WO 2003-CA1470
     20030925.  PRIORITY: US 2002-PV413171 20020925.
AB   The present invention relates to a GLP-1 peptide
     having the following formula, or a pharmaceutically acceptable salt
     thereof: X-His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-
     Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-Y (SEQ ID NO.1),
     wherein X is a rigidifying hydrophobic moiety and wherein Y is selected
     from the group consisting of OH, NH2 and Gly-OH.  Moreover, the present
     invention relates to pharmaceutical compns. comprising a therapeutically
```

Searched by: Mary Hale 571-272-2507 REM 1D86

effective amount of a peptide of the present invention, or a pharmaceutically acceptable salt thereof, in association with at least one constituent selected from a pharmaceutically acceptable carrier, diluent, and excipient.

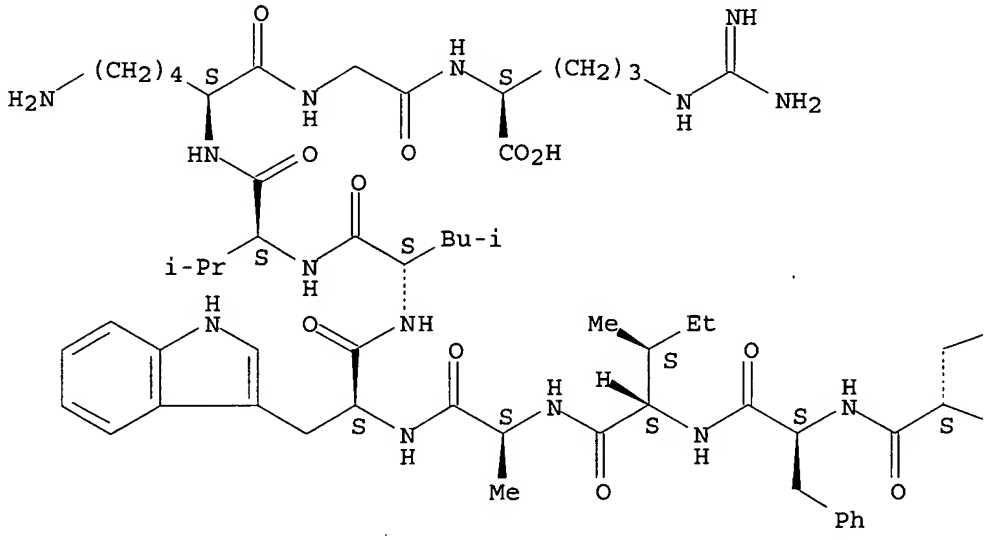
IT **676471-10-6 676471-11-7 676471-12-8**
676471-16-2 676471-17-3 676471-18-4
676471-19-5 676471-20-8 676471-22-0
676471-23-1 676471-25-3 676471-26-4
676471-27-5 676471-40-2 676471-41-3
676471-42-4 676471-49-1 676471-50-4
676471-51-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modified **GLP-1** peptides with increased biol. potency in the treatment of glucose metabolism disorders, insulin resistance, and related conditions)

RN 676471-10-6 CAPLUS

CN L-Arginine, N-(2-methylbenzoyl)-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



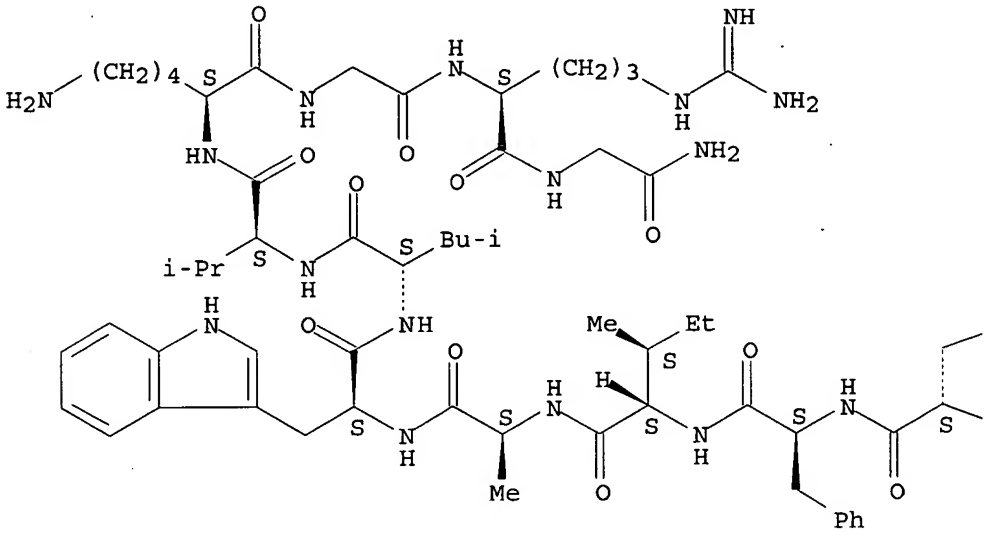
Searched by: Mary Hale 571-272-2507 REM 1D86

```
=> s gravel, d?/au;s peri, k?/au;s abribat, t?/au;s habi, a?/au
L7          108 GRAVEL, D?/AU


L8           55 PERI, K?/AU


L9           36 ABRIBAT, T?/AU


L10          12 HABI, A?/AU

=> s l7 and l8 and l9 and l10
L11           1 L7 AND L8 AND L9 AND L10

=> s l11 not l6
L12           0 L11 NOT L6

=> s l5 and (l7 or l8 or l9 or l10)
            312 L5
L13           2 L5 AND (L7 OR L8 OR L9 OR L10)

=> s l13 not l11
L14           1 L13 NOT L11

=> d cbib abs hitstr

L14  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
2002:107371   Document No. 136:161700  Modified biological peptides with
     increased potency for use in treating pathologies related to insulin
     resistance, glucose intolerance and/or type II diabetes.  Gravel,
     Denis; Habi, Abdelkrim; Abribat, Thierry
     (Theratechnologies Inc., Can.).  PCT Int. Appl. WO 2002010195 A2 20020207,
     77 pp.  DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,
     BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB,
     GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
     LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
     RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,
     ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG,
     CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR,
     NE, NL, PT, SE, SN, TD, TG, TR.  (English).  CODEN: PIXXD2.  APPLICATION:
     WO 2001-CA1119 20010802.  PRIORITY: US 2000-PV222619 20000802.
AB   The present invention is concerned with modified biol. peptides providing
     increased potency, prolonged activity and/or increased half-life thereof.
     The modification is made via coupling through an amide bond with at least
     one conformationally rigid substituent, either at the N-terminal of the
     peptide, the C-terminal of the peptide, on a free amino or carboxyl group
     along the peptide chain, or at a plurality of these sites.  Those peptides
     exhibit clin. usefulness for example in treating states of insulin
     resistance associated with pathologies such as type II diabetes.
IT   397288-62-9
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (modified biol. peptides with increased potency for use in treating
        pathologies related to insulin resistance, glucose intolerance and/or
        type II diabetes)
RN   397288-62-9  CAPLUS
CN   Glycinamide, N-[(2-methylphenyl)acetyl]-L-histidyl-L-alanyl-L-α-
     glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-

Searched by: Mary Hale 571-272-2507 REM 1D86
```

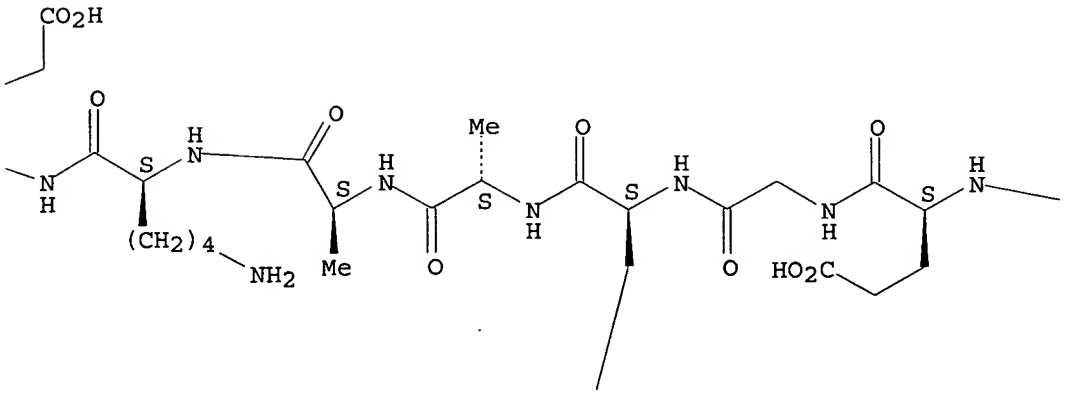
aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

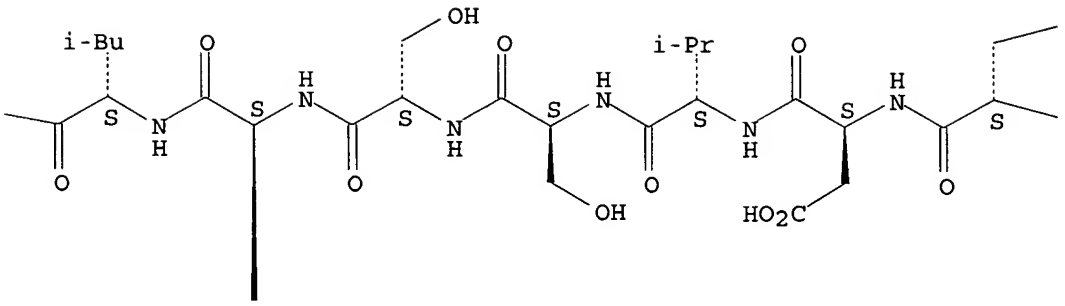
PAGE 1-A

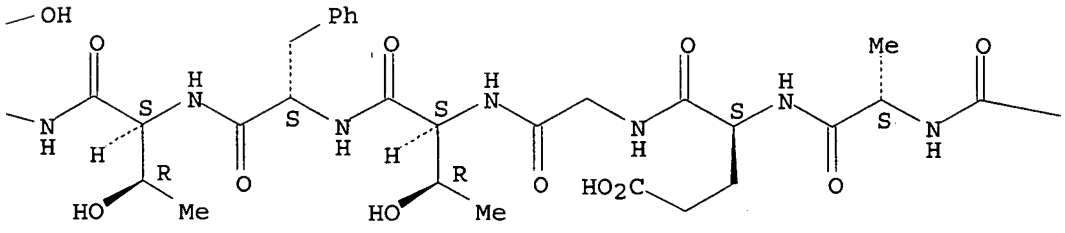


PAGE 1-B

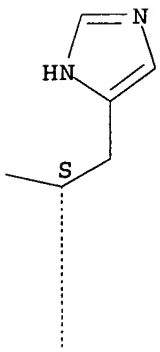


Searched by: Mary Hale 571-272-2507 REM 1D86

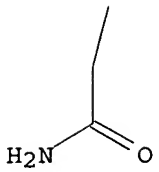

i-Bu
OH
i-Pr
OH
HO2C


OH
Ph
Me
HO
Me
HO
Me
HO2C

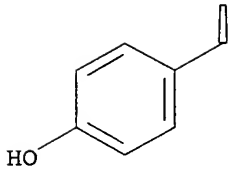
PAGE 1-E



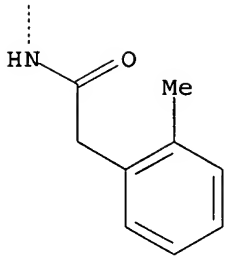
PAGE 2-B



PAGE 2-C



Searched by: Mary Hale 571-272-2507 REM 1D86



=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	30.86	189.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.40	-1.40

FILE 'REGISTRY' ENTERED AT 13:46:54 ON 30 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 DEC 2004 HIGHEST RN 805206-90-0
DICTIONARY FILE UPDATES: 29 DEC 2004 HIGHEST RN 805206-90-0

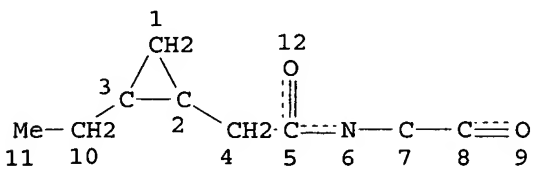
TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> => d l17 que stat;fil caplus;s l17
L15 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

Searched by: Mary Hale 571-272-2507 REM 1D86

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE
L17 10 SEA FILE=REGISTRY SSS FUL L15

100.0% PROCESSED 1024 ITERATIONS 10 ANSWERS
SEARCH TIME: 00.00.01

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	156.26	346.11

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.40

FILE 'CAPLUS' ENTERED AT 13:48:24 ON 30 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 30 Dec 2004 VOL 142 ISS 1
FILE LAST UPDATED: 29 Dec 2004 (20041229/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L18 2 L17

=> d 1-2 cbib abs hitstr

L18 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
2004:287858 Document No. 140:298100 Modified GLP-1 peptides with increased biol. potency in the treatment of glucose metabolism disorders, insulin resistance, and related conditions. Gravel, Denis; Peri, Krishna; Abribat, Thierry; Habi, Abdelkrim (Theratechnologies Inc., Can.). PCT Int. Appl. WO 2004029081 A2 20040408, 47 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-CA1470 20030925.

Searched by: Mary Hale 571-272-2507 REM 1D86

PRIORITY: US 2002-PV413171 20020925.

AB The present invention relates to a GLP-1 peptide having the following formula, or a pharmaceutically acceptable salt thereof: X-His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-Y (SEQ ID NO.1), wherein X is a rigidifying hydrophobic moiety and wherein Y is selected from the group consisting of OH, NH2 and Gly-OH. Moreover, the present invention relates to pharmaceutical compns. comprising a therapeutically effective amount of a peptide of the present invention, or a pharmaceutically acceptable salt thereof, in association with at least one constituent selected from a pharmaceutically acceptable carrier, diluent, and excipient.

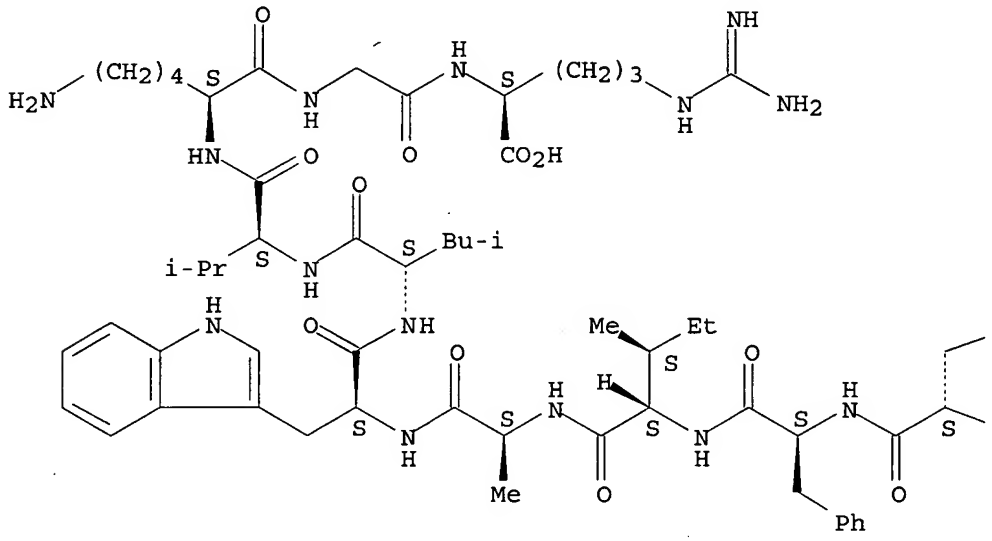
IT **676471-43-5 676471-44-6 676471-45-7**
676471-46-8 676471-47-9 676471-48-0
676540-56-0 676540-57-1 676540-58-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modified GLP-1 peptides with increased biol. potency in the treatment of glucose metabolism disorders, insulin resistance, and related conditions)

RN 676471-43-5 CAPLUS

CN L-Arginine, N-[[(1R,2R)-2-ethylcyclopropyl]acetyl]-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysylglycyl- (9CI) (CA INDEX NAME)

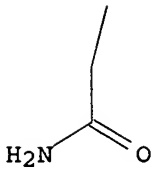
Absolute stereochemistry.

PAGE 1-A

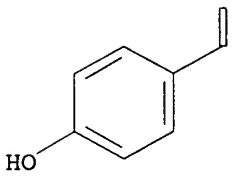


Searched by: Mary Hale 571-272-2507 REM 1D86

PAGE 2-B



PAGE 2-C



L18 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

2002:107371 Document No. 136:161700 Modified biological peptides with increased potency for use in treating pathologies related to insulin resistance, glucose intolerance and/or type II diabetes. Gravel, Denis; Habi, Abdelkrim; Abribat, Thierry (Theratechnologies Inc., Can.). PCT Int. Appl. WO 2002010195 A2 20020207, 77 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-CA1119 20010802. PRIORITY: US 2000-PV222619 20000802.

AB The present invention is concerned with modified biol. peptides providing increased potency, prolonged activity and/or increased half-life thereof. The modification is made via coupling through an amide bond with at least one conformationally rigid substituent, either at the N-terminal of the peptide, the C-terminal of the peptide, on a free amino or carboxyl group along the peptide chain, or at a plurality of these sites. Those peptides exhibit clin. usefulness for example in treating states of insulin resistance associated with pathologies such as type II diabetes.

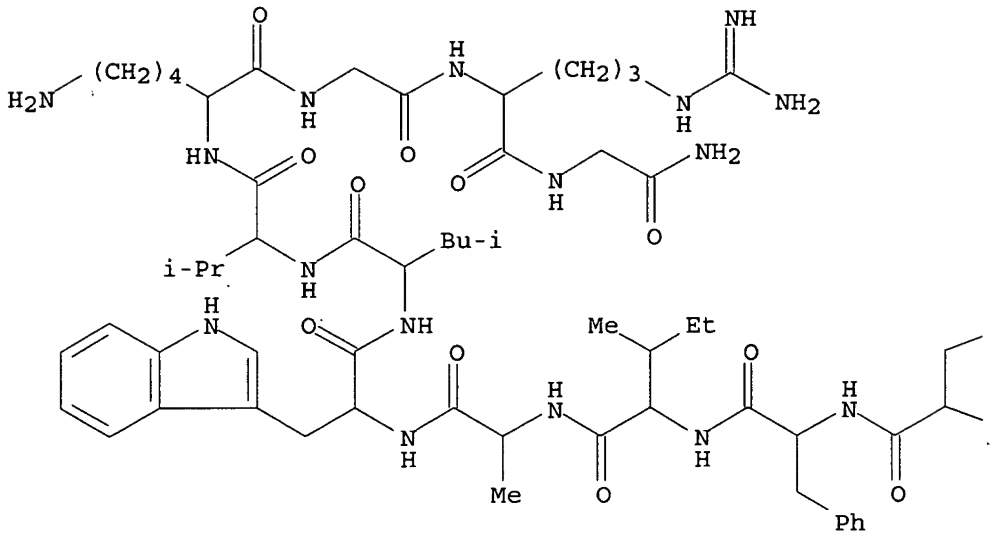
IT **397288-65-2**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(modified biol. peptides with increased potency for use in treating pathologies related to insulin resistance, glucose intolerance and/or type II diabetes)

RN 397288-65-2 CAPLUS

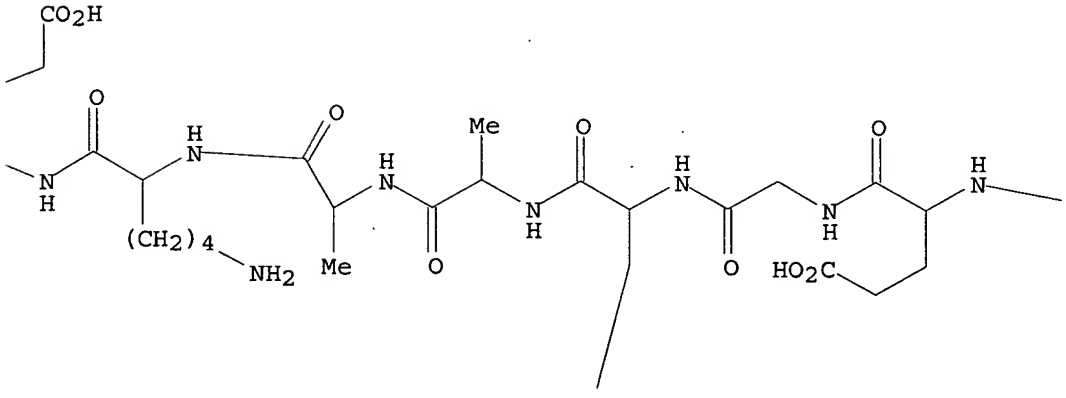
CN Glycinamide, N-[[[rel-(1S,2S)]-2-ethylcyclopropyl]acetyl]-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

Searched by: Mary Hale 571-272-2507 REM 1D86

PAGE 1-A

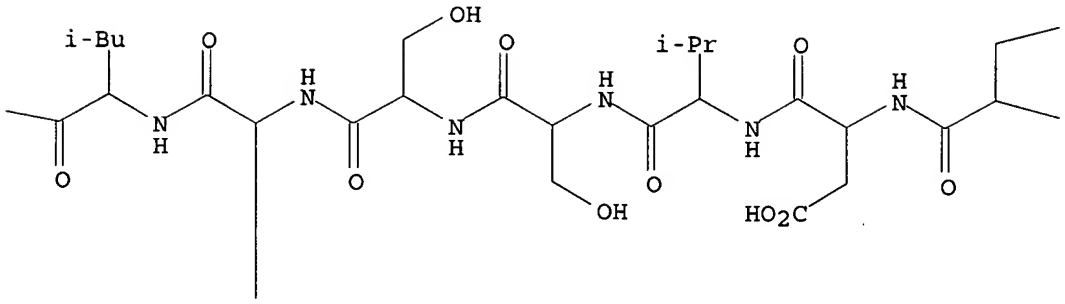


PAGE 1-B

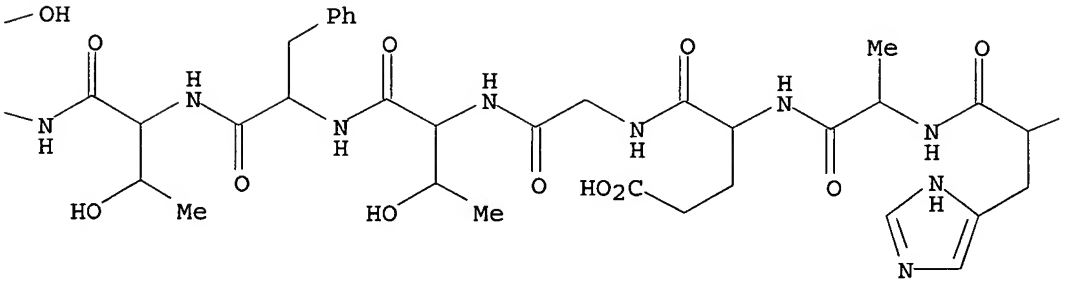


Searched by: Mary Hale 571-272-2507 REM 1D86

PAGE 1-C

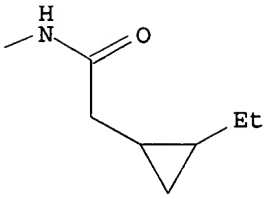


PAGE 1-D

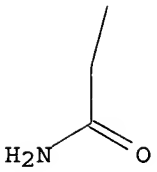


Searched by: Mary Hale 571-272-2507 REM 1D86

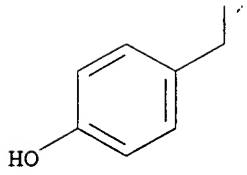
PAGE 1-E



PAGE 2-B



PAGE 2-C



=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	9.96	356.07

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.40	-2.80

STN INTERNATIONAL LOGOFF AT 13:48:33 ON 30 DEC 2004

Searched by: Mary Hale 571-272-2507 REM 1D86